Supplementary Figure legends

Supplementary figure 1. The LXR-IDOL pathway targets the LDLR membrane pool for lysosomal degradation. (**A**) HeLa cells were cultured as indicated in the presence or absence of 2μM of the synthetic LXR agonist GW3965 for four hours and 100nM Bafilomycin A1. LDLR at the cell surface was determined by FACS analysis. Cell surface LDLR in sterol-depletion medium was set to 100% (n=6, * $p<0.01$) (**B**) HepG2 cells were cultured in sterol-depletion medium in the presence or absence of 2μM of the synthetic LXR agonist GW3965 for four hours and 100nM Bafilomycin A1 or 10mM NH_4Cl. Total cell lysates were analyzed by immunoblotting as indicated.

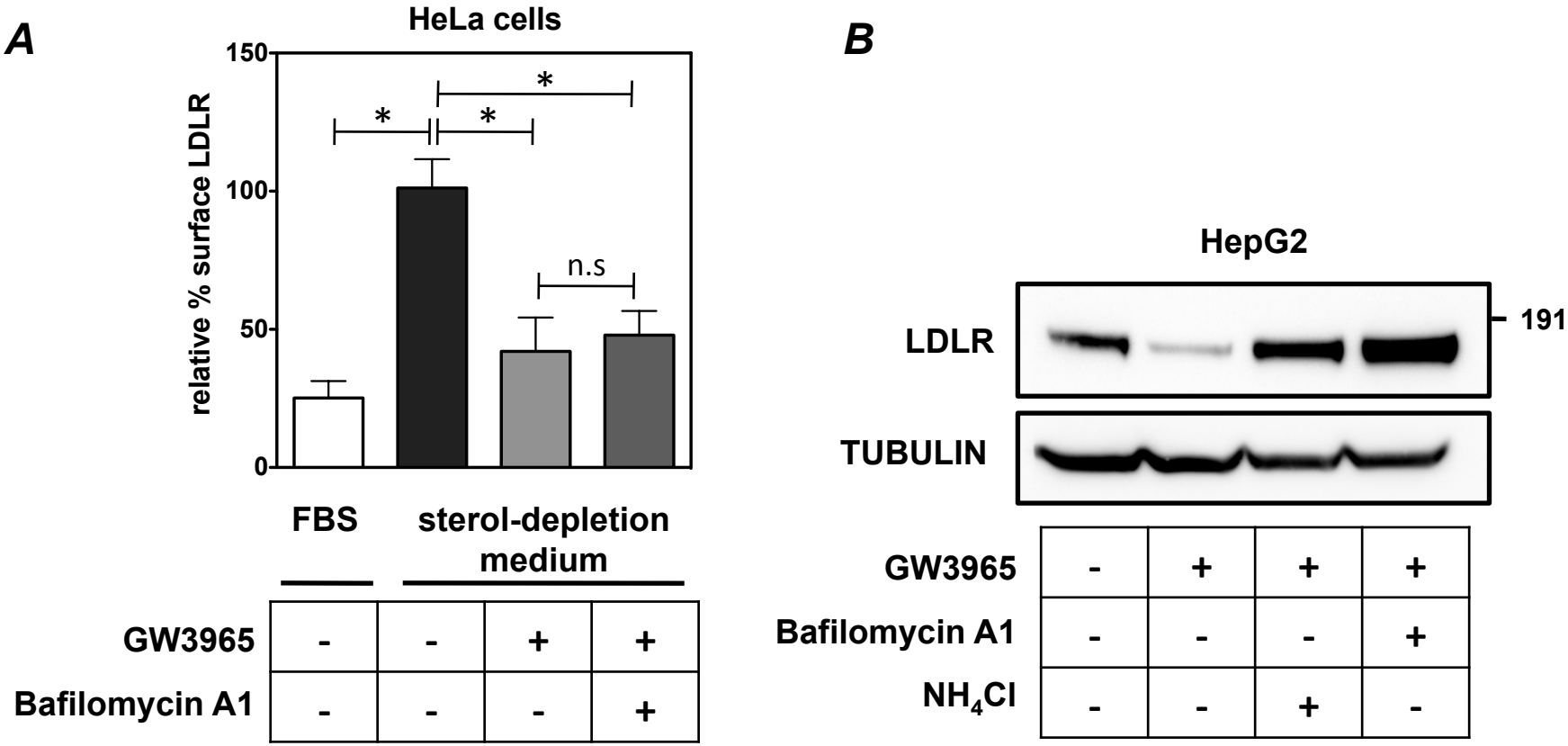
Supplementary figure 2. ARH is not required for degradation of the LDLR by IDOL. Fibroblasts in which WT *LDLR* or Y828C *LDLR* were stably introduced were incubated for 30 minutes with 5μg/mL DyLight 488-labeled LDL. Internalized LDL was quantified by measuring fluorescence in total cell lysates. LDL uptake in WT LDLR cells was set to 100%. Each bar and error represent the average ± SD (n=3, * $p<0.01$). (**B**) HepG2 cells were transfected with 20nM of control or *ARH* siRNA and subsequently incubated for 16 hours with sterol-depletion medium followed by treatment with vehicle or 1μM GW3965 for 6 hours. Total cell lysates were analyzed by immunoblotting as indicated.

Supplementary figure 3. IDOL-stimulated degradation the LDLR does not require dynamin. (**A,B**) A431 and (**C,D**) HeLa cells were incubated for 16 hours in sterol-depletion medium. Subsequently, cells were treated with 1μM GW3965 or vehicle in the presence or absence of 80 μM Dynasore for 4 hours. Total cell lysates were analyzed by immunoblotting. A representative immunoblot of two independent experiments is shown (**A,C**). For LDL uptake (**B,D**) cells were incubated for 30 minutes with 5μg/mL DyLight 488-labeled LDL. Internalized LDL was quantified by measuring fluorescence in total cell lysates. LDL uptake in vehicle-treated cells was set to 100%. Each bar and error represent the average ± SD (n=4, * $p<0.01$ from vehicle treated cells).

Supplementary figure 4. The LXR-IDOL degradation pathway targets a lipid-raft resident LDLR pool. HepG2 cells were cultured in sterol-depletion medium with vehicle or 1μM GW3965 for 4 hours. Membrane fractions were isolated and an equal amount of protein per fraction was separated by SDS-PAGE and immunoblotted as indicated.

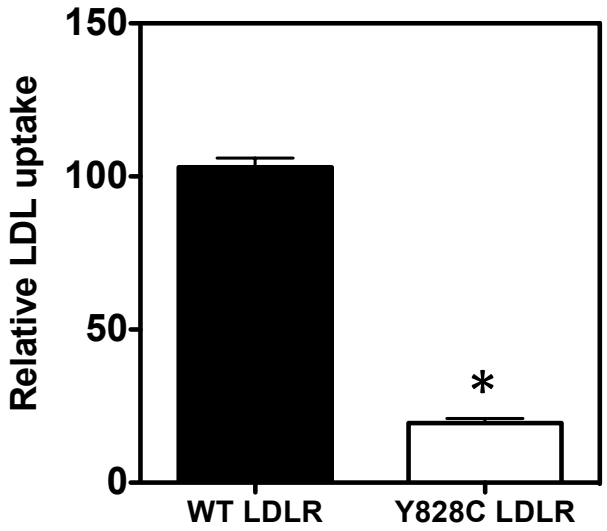
Supplementary figure 5. Epsin1 over-expression blocks IDOL-mediated degradation of the VLDLR and leads to accumulation of ubiquitylated receptor. (**A**) HEK293T cells were transfected with expression plasmids for VLDLR-HA, FLAG-IDOL, Myc-rEpn1, and GFP to monitor transfection efficiency. Samples were immunoprecipitated and analyzed by immunoblotting as indicated.

Sorrentino *et al.* Supplementary figure 1



Sorrentino *et al.* Supplementary Figure 2

A



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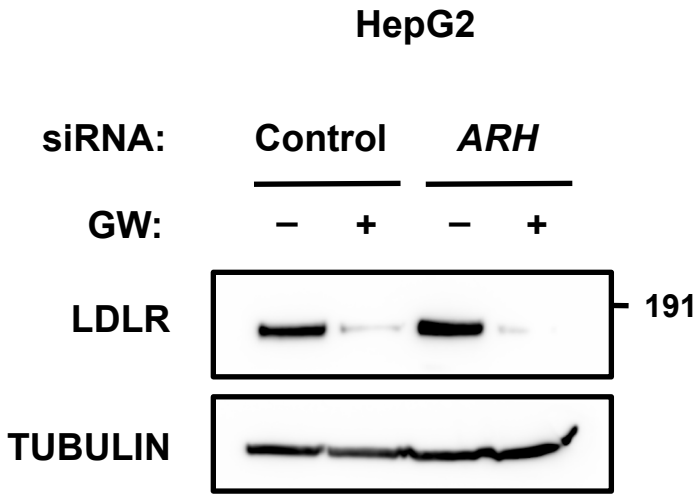

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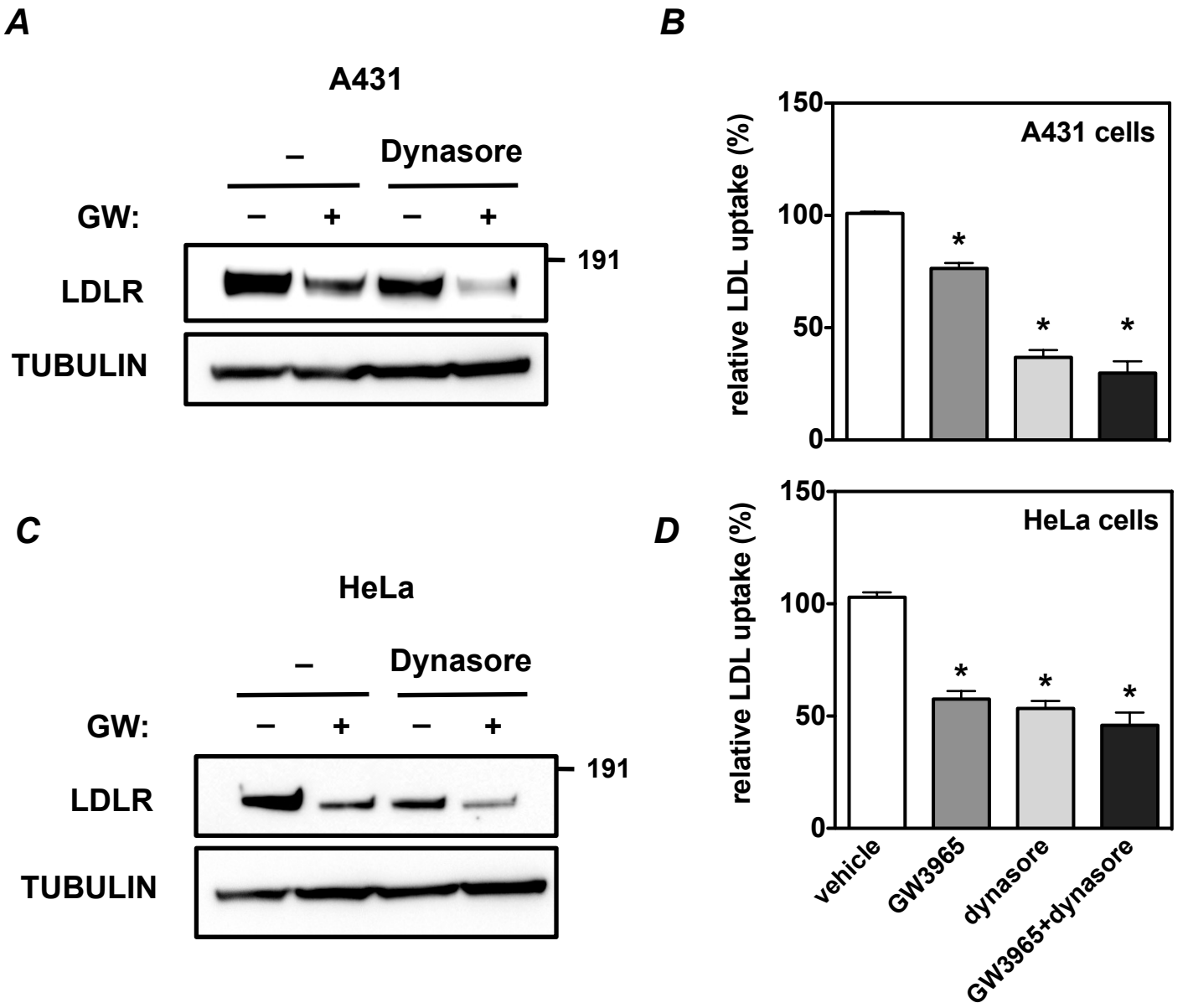

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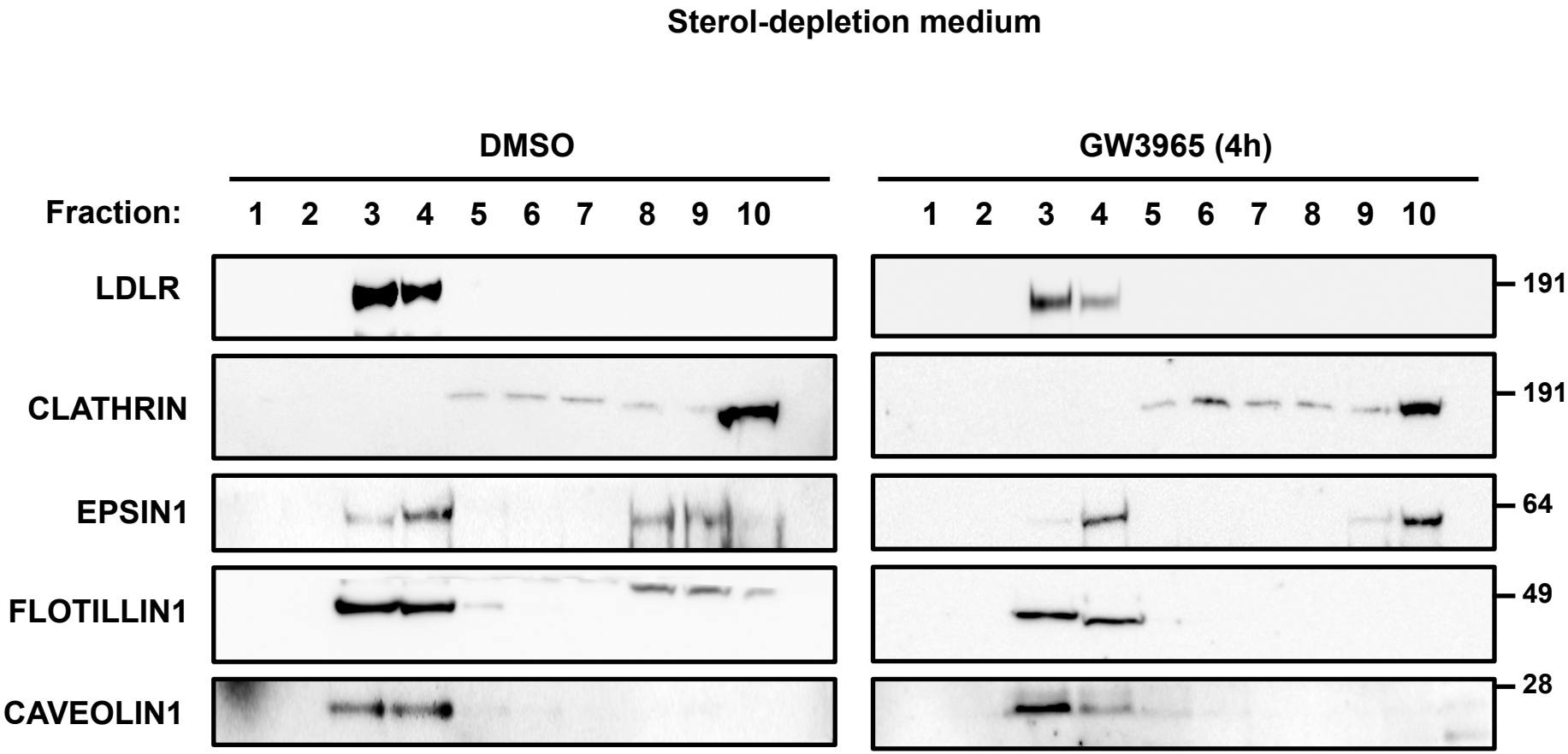

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